

**REMARKS**

With entry of this amendment, claims 53-56 are pending in the application. By this amendment, claims 53, 55, and 56 have been amended for clarity to correct formal errors, without changing the scope of the claims, and without prejudice. Claims 1-52 were previously canceled without prejudice, and Applicants continue to reserve the right to pursue the subject matter of these canceled claims in one or more related applications. All of the amendments herein are fully supported by the disclosure, and no new matter has been added to the application.

Patentability Under 35 USC § 112

Claims 53-56 are rejected under 35 USC § 112 for alleged failure to comply with the written description requirement. Specifically, the Office contends that the claims present new matter in the recitation of the term “organic eluent”, which is allegedly not supported on the basis that the disclosure fails to specify that “any and/all organics is applicable as eluent in the instant process.”

Applicants respectfully traverse the foregoing rejection and submit that the disclosure adequately conveys the subject matter of the invention in a manner sufficient to fulfill the written description requirements of 35 USC § 112.

It is unquestionable from the record that the term “new matter” cannot properly be applied to the allegedly objectionable claim term “organic eluent.” This term is used throughout the specification (see, e.g., p. 7, lines 35 and 41), in its ordinary and customary meaning, and therefore cannot be objected to on this statutory basis. New matter, by definition, is subject matter introduced into the claims or specification after the filing date of the application.

The rejection for alleged lack of written descriptive support, as advocated by the Office, would limit Applicants’ invention to utilizing a single organic solvent “hexaneisopropyl (95.5) and diethylamine (0.05%)” as advocated by the Office (Office Action at p. 2). Clearly, this is neither a practical boundary for protection of the

invention, nor would such limitation comport with the knowledge and understanding of those skilled in the chemical arts.

Applicants' disclosure closely clearly teaches that a range of useful organic eluents can be used within the subject method step, and this disclosure will be readily understood by those skilled in the art. For example, the specification teaches (beginning at p. 7, line 41) that:

The preferred eluent is a hydrocarbon solvent adjusted in polarity with a miscible polar organic solvent." Preferably, the organic eluent contains a non-polar, hydrocarbon solvent present in about 95% to about 99.5% (volume/volume) and a polar organic solvent present in about 5 to about 0.5% (volume/volume). In a preferred embodiment, the hydrocarbon solvent is hexane and the miscible polar organic solvent is isopropylamine.

In order to support the instant rejection, the Office bears the burden of establishing that any contested subject matter set forth in the claims is not, in fact, supported by an adequate written description. In re Wertheim, 191 USPQ 90, 98 (CCPA 1976). The adequacy or inadequacy of the disclosure must be weighed in light of the understanding possessed by persons skilled in the art. In re Hayes Microcomputer Products Inc., 25 USPQ2d 1241, 1245 (CAFC 1992). The specification "does not have to describe exactly the subject matter claimed . . ." Vas Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (CAFC 1991). Rather, the specification "need only convey to one of skill in the art, in any manner, that a later added claim limitation was part of applicants' invention." Ex parte Anderson, 21 USPQ2d 1241, 1249 (Bd. Pat. App. Inter. 1991) (relying on In re Smythe, 178 USPQ 279, 284 (CCPA 1973)).

In the instant case, Applicants' claims are ambiguously rejected for allegedly presenting "new matter" by recitation of the claim term "organic eluent"—which the Office contends is only described as a single species ("hexaneisopropyl (95.5) and diethylamine (0.05%)"). The foregoing teachings cited from the disclosure clearly refute the Offices' position and demonstrate fully adequate descriptive support for the allegedly objectionable term "organic eluent". Not only does the disclosure clearly convey the metes and bounds of this term (notably the rejection was not presented based on alleged "indefiniteness"), but the description clearly evinces that the term "organic eluent" was

presented, and would be readily understood, as “part of applicants' invention” at the time the application was filed.

In view of the foregoing, the rejection of claims 53-56 under 35 USC § 112 is believed to be overcome.

Patentability Under 35 USC § 103

Claims 53-56 are rejected under 35 USC § 103 as allegedly unpatentable over Miller et al., J. Chrom. A, (1999) Vol. 865, pp. 211-226. The Office relies upon Miller et al. for allegedly disclosing “a process for separating a racemic mixture with chiral polysaccharide stationary phase and polar organic solvents a (sic) eluent.” The Office states that the difference between the instant invention and that of Miller et al. is that the current claims are directed toward resolving a racemic mixture of -1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane, whereas Miller et al. is directed to “racemates”. The Office further contends that the term “racemates” as used by Miller et al., “embraces the racemate mixture of -1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane”, and that on this basis the instant invention is allegedly *prima facie* obvious.

Applicants respectfully traverse the foregoing grounds of rejection and submit that the article by Miller et al. neither discloses nor suggests the instantly claimed subject matter.

The foregoing rejection is facially incomplete because it posits that there is no substantive significance to the “racemate” composition to be resolved. As the Office presents the rejection, the method of Miller et al. would have to meet a standard that it “embraces the racemate mixture” of any and all compounds. This reasoning is facially untenable, and does not meet the standard of review that the PTO must apply.

To adequately support the instant rejection, the Office must provide direct scientific evidence that a cited reference, or combination of references, teaches or practically motivates the independent discovery of every element and limitation in the claims presented for review.

In this case, the Office must show that Miller et al. provides sufficient practical motivation that would lead the skilled artisan, “with a reasonable expectation of success”

to isolate virtually any enantiomer from a racemic mixture--regardless of its specific identity and properties.

This burden must be met with an even greater breadth of presumption based on the general characterization of Miller's method by the Office as employing "polar organic solvents with polysaccharide stationary phase." Said alternatively, the Office must validate a position that ALL such generic methods (i.e., employing any polar organic solvent and any polysaccharide stationary phase), would be considered to provide "a reasonable expectation of success" for resolving any and all enantiomers—regardless of the nature and characteristics of the subject enantiomer.

On the instant record, the basis for the asserted *prima facie* case of obviousness is simply incomplete. Only a single reference is cited, for teaching a generic protocol to resolve racemic mixtures. This reference makes no mention of Applicants' specific racemate, which is certainly not among the limited number of racemates successfully resolved by Miller and coworkers.

In summary, no evidence is provided in the record that would extend the generic method of Miller et al. to read on any and all racemates. No mention is provided, anywhere in the record, of the novel subject of Applicants' successful method, -1-(3,4-dichlorophenyl)-3-azabicyclo[3.1.0]hexane.

There must be a specific teaching or practical suggestion in the cited reference, or in a combination of cited references, that directly embraces Applicants' specific racemate—otherwise the rejection is facially incomplete. The only alternative construction of the current prosecution history is one that would bind the Office to a position where Miller is construed as enabling resolution of any and all racemates, and this is clearly contrary to the evidence.

Briefly, Miller and coworkers note that their method of chromatographic resolution is but one of many methods that may be selected for resolving racemic mixtures. Other known methods include recrystallization, enzymatic resolution, indirect chromatographic resolution, and other forms of direct chromatographic resolution. Miller and colleagues further note that many variables affect the utility of different resolution methods, including whether diastereomers or enantiomers are targeted, whether the resolution is analytical or preparative, and whether the method is direct or indirect (the

latter requiring additional steps and thereby providing less predictability). Additional variables include, notably, solubility of the targeted racemic mixture in “traditional mobile phases”, such as “an alcohol-hydrocarbon combination”. If performance in such traditional mobile phases is poor, it might then be useful to employ non-traditional methods.

This latter point is particularly relevant to the instant rejection, because Miller et al. expressly emphasize the non-traditional nature of their methodology. At page 212, left column, the authors specifically contrast their methods with those that employ traditional, alcohol-hydrocarbon mobile phases. In this context, Miller and colleagues qualify the level of knowledge pertaining to their method by stating as follows: “Initial work has been reported on the use of polar organic solvents (methanol, ethanol, acetonitrile) with polysaccharide based CSPs [14, 15].”

The nature of this representation facially contravenes the Office’s proposal that the use of a polar solvent and polysaccharide based chiral stationary phase (CSP) would be appreciated as a universally applicable method for resolving any and all racemic mixtures. In fact, the Miller reference itself teaches that only “initial work” had been provided up to that point using these combined techniques--and the Miller team clearly fails to advance these initial teachings to yield a universally applicable method as would have to be proved by the Office.

Without question, the Miller et al. disclosure fails to satisfy the burden imposed on the Office--to show that all elements and limitations of Applicants’ claims are either directly disclosed, or specifically suggested, by one or more references of record. To overcome the requirement for such a specific suggestion, the only prospect to satisfy this burden would be to show that Miller et al. teach “a reasonable expectation of success” for using a generic combination of a polar solvent and a polysaccharide based chiral stationary phase to resolve ALL enantiomers from ALL racemic mixtures. This position is simply untenable, and it is refuted by a host of uncertainties in the technical field surrounding the invention.

Although the instant response is believed to be sufficient and fully responsive on the grounds presented, Applicants reserve the right to present additional evidence pertaining to such uncertainties, if required, later in prosecution. In addition, the Office is

asked for the purpose of this response to take notice of such evidence, e.g., pertaining to the scope and reliability of the Miller et al. method as applied to diverse racemic mixtures, as may later be shown by Applicant to be widely known and understood in the art.

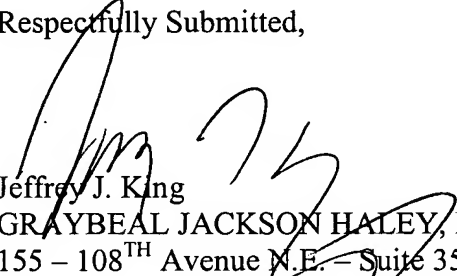
In view of the foregoing, Applicants respectfully request that the rejection of claims 53-56 under 35 USC § 103 as allegedly unpatentable over Miller et al., J. Chrom. A, (1999) Vol. 865, pp. 211-226, be withdrawn.

### CONCLUSION

In view of the foregoing, Applicants believe that all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at (425) 455-5575.

Respectfully Submitted,



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